

**FACILITIES & OTHER RESOURCES – LIFESPAN HEALTH SYSTEM**  
**Including: Rhode Island, Hasbro Childrens, The Miriam and Bradley Hospitals**

**LIFESPAN SYSTEM HOSPITALS**

Lifespan, Rhode Island's first healthcare system, was founded in 1994 by Rhode Island Hospital and The Miriam Hospital. A comprehensive, integrated, academic health system affiliated with The Warren Alpert Medical School of Brown University, Lifespan's present partners also include Rhode Island Hospital's pediatric division, Hasbro Children's Hospital; Bradley Hospital; Newport Hospital and Gateway Mental Health Services. A not-for-profit organization, Lifespan is overseen by a board of volunteer community leaders who are guided by its mission: Delivering Health with Care.

**Rhode Island Hospital:** Rhode Island Hospital, with 750 beds, is the state's largest hospital and the third largest hospital in New England. It is designated as the Level 1 Trauma Center for southeastern New England, providing expert staff and equipment in emergency situations 24 hours a day. Rhode Island Hospital provides comprehensive diagnostic and therapeutic services to inpatients and outpatients, with particular expertise in cardiology, oncology, neurosciences and orthopedics, as well as pediatrics at its Hasbro Children's Hospital. Rhode Island Hospital is home to a Comprehensive Cancer Center. Its pediatric division, Hasbro Children's Hospital, opened in 1994 and cares for some 7,000 inpatients and 60,000 outpatients annually. Two distinct emergency departments exist on the RIH campus: the Andrew F. Anderson Emergency Center and Hasbro Children's Hospital ED's. The annual patient volume of these facilities is over 130,000 patient visits per year. Both ED's also house the American College of Surgeons approved Level 1 trauma center. The new Anderson Emergency Center was constructed in 2005 and encounters > 80,000 adult visits per year and is the tertiary care referral site for all of southeastern New England. Both ED's sponsor highly regarded PGY1-4 residency programs in emergency medicine with 48 residents in training and a pediatric emergency medicine fellowship. There are over 3000 new cancer cases diagnosed each year at RIH. The hospital has a new, state-of-the-art, cancer center integrating radiation oncology and medical oncology within three adjacent floors of the Ambulatory Patient Care (APC) building of Rhode Island Hospital. Full imaging facilities, including CT scan, MRI, PET scan, and other diagnostic imaging is directly connected to the cancer center via a walkway to the main patient building. There is a dedicated inpatient oncology floor on the fourth floor building. There is a dedicated hematology/oncology ward team who follows the inpatient service. This includes a hematology oncology attending, fellow, two medical residents, a pharmacist and 1-2 Brown Medical students. RIH participates in cooperative group, pharmaceutical and investigator initiated studies. The oncology research office has 17 full-time employees. The IRB meets twice a month.

**Hasbro Children's Hospital:** Hasbro Children's Hospital is deeply committed to advancing medical knowledge and improving patient care for children through the latest research. It currently has 53 principal investigators conducting more than 160 research initiatives, which are coordinated across Hasbro Children's Hospital, Bradley Hospital and Women & Infants Hospital and The Warren Alpert Medical School of Brown University. Hasbro researchers have made significant findings in cancer, liver disease, diabetes and asthma, and our research has appeared in more than 500 publications over the past five years. Pediatric cancer research is led by members of the Children's Oncology Group. In FY2010, total research funding among Hasbro Children's Hospital, Bradley Hospital and Women & Infants Hospital was \$23.5 million.

**The Miriam Hospital:** The Miriam Hospital is a 247-bed facility that provides a broad range of primary, secondary and tertiary medical and surgical services to adolescents and adults in 31 medical and surgical specialties and sub-specialties. The hospital provides a broad range of primary, secondary, and tertiary medical and surgical services. Miriam Hospital is noted for its specialty services in AIDS at the Samuel and Esther Chester Immunology Center and in cardiac care. The Women's Cardiac Center at The Miriam Hospital offers complete diagnostic and clinical cardiology services, cardiovascular surgery and cardiac rehabilitation to women. The Miriam Hospital is a major teaching hospital affiliated with Brown University. The hospital is home to (1) The Immunology Center, (2) the Sexually Transmitted Disease (STD) Clinic, (3) the Pre-Exposure Prophylaxis (PrEP) Program, (4) the Centers for AIDS Research (CFAR), (5) The Immunology Center Research Laboratory, and (6) the Centers for Behavioral and Preventive Medicine.

**Emma Pendelton Bradley Hospital:** The Emma Pendelton Bradley Hospital, founded in 1931, is the nation's first psychiatric hospital devoted to children and adolescents. It is the nation's only free-standing child/adolescent psychiatric hospital. Bradley services include a 60-bed acute inpatient program for children and adolescents with emotional, behavioral, and developmental disorders and outpatient services (including a

dialectical behavior therapy [DBT] program), day treatment, and five fully certified special education schools across RI for youth with psychiatric disorders.

## **LIFESPAN INSTITUTES, CENTERS, INITIATIVES AND PROGRAMS**

**Norman Prince Neurosciences Institute:** The Norman Prince Neurosciences Institute unites Rhode Island's best minds in brain science to improve health and extend life for patients with Alzheimer's disease, autism, traumatic brain injury and other diseases and disorders of the brain and nervous system. As the clinical arm of the Brown Institute for Brain Science, the internationally recognized research program at Brown University, the Norman Prince Neurosciences Institute brings together the state's leading experts in neurosurgery, neurology and psychiatry and connects them with the top brain scientists at Brown. These clinical scientists are members of The Warren Alpert Medical School of Brown University and work in its affiliated hospitals, including: Rhode Island Hospital and its Hasbro Children's Hospital, Butler Hospital, Bradley Hospital and the Providence VA Medical Center.

The Norman Prince Neurosciences Institute is dedicated to advancing the neurosciences and reducing human suffering from disorders of the nervous system through world-class research, outstanding clinical care and advanced education. The goals of the institute are to 1) Conduct rigorous, innovative research that unites and leverages the strengths of its partners - Rhode Island Hospital and its Hasbro Children's Hospital, Butler Hospital, Bradley Hospital, Brown University and the Providence VA Medical Center, 2) Provide exceptional clinical care delivered with compassion and informed by current, cutting-edge science and 3) Educate a new generation of physicians and scientists to conduct collaborative, creative science and deliver the highest caliber medical care. The institute was established in 2010 with a \$15 million gift from the Frederick Henry Prince 1932 Trust, which was created by Norman Prince's father, Frederick Henry Prince, a Boston entrepreneur. The gift from the trust to Rhode Island Hospital was the single largest gift in the hospital's history

**Dana-Farber and Lifespan Cancer Institute** support the expansion of clinical trials, access for Lifespan physicians to cancer-specific disease expertise for complex cases, and the launch of a new program to coordinate the treatment of bone marrow transplant patients, with transplants provided in Boston at Dana-Farber/Brigham and Women's Cancer Center, and care surrounding the transplant provided at Lifespan Cancer Institute in Providence. Dana-Farber Cancer Institute and the Lifespan Cancer Institute have created a strategic alliance to advance cancer treatment and research. The collaboration will be made easier, they said, by Lifespan and Dana-Farber's common cancer-specific electronic health record system, the Epic Beacon platform, as well as their use of the same OnCore clinical trials management system.

A top priority of Dana-Farber and Lifespan Cancer Institute's work together is the ability to offer the latest and most advanced clinical trials to patients in Rhode Island. While many of these trials are developed at and provided by Dana-Farber, there are also opportunities for clinical trials developed at the Lifespan Cancer Institute to be offered to Dana-Farber patients. Increasing access to diverse patient populations is a common goal to help accelerate the development of new therapies. Other areas of collaboration include genomics and precision medicine, cancer disparities, innovation in the delivery of cancer care, and potential synergies in basic research. The two organizations have collaborated on a multi-site grant application for genomics with a health disparities component.

**Precision Medicine** uses genomic and proteomic information, alongside environmental and lifestyle information, to create a comprehensive dataset for personalizing disease treatment, management, and risk mitigation. Based on early successes, it is anticipated that precision medicine will extend beyond cancer to high-prevalence problems such as autism and neurodegeneration, and will improve the long-term health and quality of life for entire populations. Because better understanding of the individual leads to more effective prevention and treatment of illness, a statewide initiative in precision medicine has been developed within Advance-CTSA that includes coordinated efforts in personalized cancer care, risk assessment strategies throughout the lifespan, and a broad multidisciplinary coordinated support of research in precision medicine.

**The role of precision diagnostics in personalized cancer care** has shown dramatic progress nationwide, with molecular signatures a critical component of many cancer care decisions. In a strategic alliance with the Dana Farber Cancer Institute (DFCI), the Lifespan Cancer Institute (LCI) is developing shared approaches to personalized care and have already submitted combined research applications. Two Next Generation Sequencing instruments (Illumina MiSeqDX and Illumina NextSeq) for genomic testing have been purchased and multi-gene panel testing for lung and colorectal cancer on the Agena MassARRAY platform (MALDI-TOF mass spec), as well as individual testing for mutations in KRAS, BRAF, and EGFR are offered. LCI's

biorepository includes frozen tumor samples, cultured cancer cells, and pre-operative blood samples, and LCI and DFCI have developed strategies for standardized classification, genomic testing, reporting, and data-mining that will create a regional cancer cohort for coordinated clinical trials with a single approach to proteogenomic assessment and diagnosis. As one example, Medley Genomics, a startup company that developed from our group, uses advanced algorithms to describe genomic cellular heterogeneity and will validate these algorithms in coordination with LCI, supported in part by an investment from the state's RI Commerce Corporation.

**Prenatal assessment** uses cell-free DNA of maternal plasma as part of its comprehensive screening for fetal health within our DHHS-designated National Center of Excellence in women's health. Pregnant women receive risk scores for common aneuploidies (e.g. trisomies 21, 18, 13), and newer technologies will include microdeletions and detection of single gene disorders. The Rhode Island Consortium for Autism Research and Treatment (RI-CART), funded by the Simons Foundation and the Advance-CTSA institutions, is striving to identify all of the estimated 10,000 Rhode Islanders with autism spectrum disorders through community engagement, and to establish the first statewide autism registry, a secure, anonymous database that includes all ASD individuals in the state and their first-degree relatives, with annotated DNA samples. For care across the lifespan, our institutions have developed a strategy that combines genomic testing with medical genetic consultation and counseling. Geneticists and genetic counselors integrate genomic screening with a comprehensive management plan for a large number of current clinical indications, and anticipate screening for risks for neurodegenerative disease, diabetes, and other chronic conditions in the near future.

**Multidisciplinary multi-institutional support for research** in computational and statistical analyses of genomic datasets is provided by the COBRE Center for Computational Biology of Human Disease (CBHD), supported by the NIGMS to serve faculty and their research programs. In coordination across Advance-CTSA, the CBHD supports researchers with experimental design and computational analyses of genomic, transcriptomic and microbiome data relevant to disease assessment, risk stratification, and algorithm developments that can advance discoveries in the basic and clinical sciences. With structured mentoring, and formative and summative evaluation programs, CBHD will development its goal of supporting junior faculty into a broader center that can advise and assist basic and clinical researchers across the RI biomedical community in the computational analyses of genomic data relevant to human disease. This comprehensive coordinated program in genome enabled analyses represents an ideal environment for training tomorrow's translational scientists about precision medicine in clinical and translational research programs.

**Comprehensive Cancer Center.** There are over 3000 new cancer cases diagnosed each year at RIH. The hospital has a new, state-of-the-art, cancer center integrating radiation oncology and medical oncology within three adjacent floors of the Ambulatory Patient Care (APC) building of Rhode Island Hospital. Full imaging facilities, including CT scan, MRI, PET scan, and other diagnostic imaging is directly connected to the cancer center via a walkway to the main patient building. There is a dedicated inpatient oncology floor on the fourth floor building. There is a dedicated hematology/oncology ward team who follows the inpatient service. This includes a hematology oncology attending, fellow, two medical residents, a pharmacist and 1-2 Brown Medical students. RIH participates in cooperative group, pharmaceutical and investigator initiated studies. The oncology research office has 17 full-time employees. The IRB meets twice a month.

**Hematology Oncology:** investigators in the Division of Hematology/Oncology occupy approximately 10000 square feet of dedicated laboratory space which includes research bench space including a microscope suite, tissue culture rooms, flow cytometry suite, heavy equipment room and a utility room with an autoclave, dishwasher and ice machine, a cold room, a radioisotope room and chemical storage room. Tissue culture facilities have 4 CO2 incubators, 5 laminar flow hoods, an inverted microscope, liquid N2 storage, a table top centrifuge and other small equipment necessary for handling cell cultures. Investigators in the division have access to a Gammacell 40 irradiator, a BD Bioscience Influx cell sorter, a BD LSR II flow cytometer, two Zeiss motorized fluorescent upright microscopes and one Zeiss inverted fluorescent microscope with a climate controlled chamber. An ABI Via VII Fast Real Time PCR system, 9800 Fast Thermocycler, a Nano drop ND/1000 spectrophotometer, Nanosight NS500 nanoparticle counter and a Bio Rad chemi-luminescent detection system. For a small fee, the RI Hospital Core Research Labs provide services in electron microscopy and confocal microscopy. Lifespan and Rhode Island Hospital have made significant commitments to its research enterprise of which the Division of Hematology/Oncology is a major part. A 10,000 square foot renovation of new laboratory space in the Coro West building has been completed.

## **Cardiovascular Institute:**

**Cardiovascular Research Center (CVRC):** The CVRC, a Brown University-sponsored entity designed to bring together all cardiovascular researchers on campus. The Cardiovascular Research Center (CVRC) is located in ~10,000 sq ft of newly renovated, state-of-the-art laboratory space in a rapidly growing center for biomedical research in Providence RI, including Alpert School of Medicine and Rhode Island Hospital labs and facilities. CVRC facilities include a sophisticated invasive animal catheterization and electrophysiology laboratory, and a brand new state-of-the-art research facility that is used for studying genetically modified mouse and rabbit models of cardiac diseases. The CVRC has 16 professor level faculty members who contribute to an open and supportive intellectual environment. Collaborations among investigators are commonplace and promote a rich environment for completion of the proposed studies. In addition, The CVRC hosts weekly methodology presentations of interest to cardiovascular and pulmonary investigators, weekly presentations of investigators data which encourage scientific communication and collaboration within the facility, and bi-monthly invited talks of distinguished visiting scientists. Importantly, numerous opportunities exist for scientific engagement and collaboration around the Alpert Medical School, School of Public Health, and RIH scientific departments including weekly research seminars in the department of Surgical Research (of which we are also members). Opportunities exist for faculty development around the Alpert Medical School campus through the Office of BioMed Faculty Affairs with monthly seminars to promote career development for all faculty levels. Examples include March: Faculty Workshop for Medical School Faculty; May: Grant-writing Workshop for all Faculties, April: Clinical Department Faculty Teaching Workshop; June Professional Development Conference.

**The Centers for Behavioral and Preventive Medicine (CBPM):** The Centers for Behavioral and Preventive Medicine aims to improve health through behavioral change and the integration of behavioral and biomedical science using clinical, community, and laboratory-based research. The Centers' research bridges biomedical, sociobehavioral, and population/public health scientific disciplines. Faculty members are committed to both basic research on discovering the mechanisms underlying behavioral factors in health and illness (e.g., examining the stress response among children and adolescents, neuroimaging of AIDS and other medical conditions), as well as to applied research on the translation of these discoveries for clinical and community health improvement. Programs range from those that focus on primary prevention (e.g., promoting tobacco cessation, preventing weight gain, increasing physical activity, and HIV/AIDS prevention) to improving the effectiveness of treatment and enhancing quality of life in populations such as cancer survivors and patients enrolled in cardiac rehabilitation programs.

**The Vascular Disease Research Center** at Rhode Island Hospital develops clinical trials and basic science research, and has a demonstrated track record in obtaining funding for these initiatives from the federal government through the National Institutes of Health (NIH). The center also coordinates a number of Food and Drug Administration (FDA). We can help investigators seeking to develop ideas in the vascular disease arena into fundable grant applications, either formally with center involvement or informally. We also can serve in this capacity for the medical device or drug industry, helping to plan and execute all aspects of FDA studies. Our mission is to advance scientific understanding and improve public health by developing and performing pivotal clinical and basic scientific research in peripheral vascular disease.

**Center for International Health Research.** To address the many urgent global health challenges, the Center for International Health Research (CIHR) at Rhode Island Hospital was founded in 2005, under the aegis of the departments of pathology and pediatrics. The Center for International Health Research (CIHR) works to understand the mechanisms that cause tropical infectious diseases, specifically malaria and schistosomiasis, and to harness this knowledge to design improved treatments and vaccines. The CIHR embraces interdisciplinary approaches by linking basic lab science with cutting edge population-based science. It is this approach that makes the center unique in Rhode Island and in southern New England.

**Lifespan Alzheimer's Disease and Memory Disorders Center.** The Center conducts major clinical trials and provides the most up to date facilities to maximize the comfort and experience of the study participants as well as their safety. There are examination rooms, two infusion rooms for administering intravenous antibodies against amyloid, a waiting area, reception area, conference room, television, snacks and coffee. A dedicated computer workstation is used for brain image analysis and driving video research. An on-site laboratory is used to handle research specimens from clinical trials and also houses the Biospecimens Donation Bank containing blood and spinal fluid specimens that are stored and frozen for future research. Research areas of interest include: (1) Clinical trials for primary and secondary prevention of Alzheimer's disease, (2)

Pharmacoepidemiology in aging and dementia, (3) Transcranial magnetic stimulation in frontotemporal dementia and degenerative brain disorders, (4) Insulin and “type 3 diabetes” in Alzheimer’s disease, (5) Biomarkers and brain imaging studies of preclinical Alzheimer’s and mild cognitive impairment, (6) Driving and other behavioral problems in MCI and AD, (7) Cognitive screening tests for mild cognitive impairment and normal aging, (8) Blood brain barrier in Alzheimer’s and mild cognitive impairment, (9) Vascular contributions to development of dementia, (10) Quality of life in dementia and caregiver support.

**Neurocognitive Program at RIH:** The active clinical program has five full-time staff neuropsychologists. Regular referral sources to the program include neurologists, internists, and psychiatrists from across the region. Three devoted examination rooms and a conference room are available for research and clinical activities. The program has an extensive library of neuropsychological test materials and computerized scoring programs. The Neuropsychology Program currently has 18 computers and several printers all connected by a local area network. The staff and several research assistants have extensive experience in database development for entering and storing large amounts of research data in a confidential and secure fashion. Rhode Island Hospital maintains a computer intranet, which allows for high speed network internet access from each desktop for authorized users. 4) Brain MRI Scanning: The Department of Diagnostic Images at Rhode Island Hospital will perform brain MR scanning for the enrolled patients with cardiac and non-cardiac vascular surgery. Our-hospital is currently equipped 4 -Siemens MR-systems. 2 sets of Siemens 1.5T MAGNETOM Aera MR systems (D13 software) with 20 Channel Head/Neck array (16ch. head, 4ch.neck) at Rooms 2 & 4 will be used for current study (research).

**Hasbro Children’s Research Center (BHCRC).** As major teaching hospitals for The Warren Alpert Medical School of Brown University, Bradley Hospital and Hasbro Children’s Hospital employ faculty who are national leaders in clinical and basic research. To centralize our efforts, promote collaboration among research groups and maximize our impact on our field, all the child mental health researchers within our two hospitals came together to form the Bradley Hasbro Children’s Research Center (BHCRC). Most of the research groups are located within a 20,000-square-foot space in Providence, but the Bradley Sleep Lab and the Bradley Campus Research Unit in East Providence also house our investigators. Centralized infrastructure, physical proximity of disparate research groups, and regular research meetings promote collaboration and cross-fertilization of research ideas. In addition, a highly successful, NIH-supported research training program within the BHCRC is producing the next generation of young investigators.

The BHCRC encompasses a broad spectrum of research programs that share a commitment to studying the impact of psychological factors on the growth and development of children and their families. Under the center’s umbrella, investigators direct over 50 externally funded projects. Grant support is extensive: awards average over \$10 million each year and the total grant awards for all years of currently active projects averages close to \$50 million. BHCRC investigators are continually seeking answers to the most important questions in the realm of child development and child mental health. We are exploring new insights into the genetic roots of autism; finding pediatric bio-behavioral markers of bipolar disorder; creating effective therapies for OCD; devising effective prevention strategies for adolescent sexual risk behaviors and obesity; and much more. Every day, we are generating new projects, testing new therapies and challenging conventional wisdom in new ways—all with the single aim of helping children develop into healthy adults. Consists of more than 50 psychiatrists, psychologists, and staff working in more than 9 research groups (including the PediMIND program) devoted to advancing what is known about psychiatric illness in children/adolescents. The Bradley/Hasbro Research Center is housed in 15,000 sq. ft. of research space, including offices, interview/testing rooms, and conference space.

**Pediatric Mood, Imaging, and NeuroDevelopment (PediMIND):** Dr. Dickstein's Pediatric Mood, Imaging, and NeuroDevelopment (PediMIND) program at Bradley Hospital. PediMIND is affiliated with both the Bradley/Hasbro Research Center and Brown University's Institute for Brain Science (IBS; a crossdisciplinary group of 100+ investigators affiliated with Brown) where projects are facilitated by energetic colleagues and resources described below located no more than 15 minutes from one another. The PediMIND program is currently housed in 5100 sq. ft. of newly renovated research-dedicated space at Bradley Hospital, including interview/assessment rooms, conference space, office space, and secure data space--all contiguous with the inpatient and outpatient facilities. Resources available via the PediMIND Program include: 1) Apple MacPro quad-core computer with 5.5 Terabyte RAID configured hard drive for behavioral and MRI data analysis with MRI analytic software (including AFNI, FSL, FreeSurfer, and MATLAB) plus parallels PC emulation software for using Microsoft Windows programs. 2) 4 PC desktop computers and 4 PC notebook computers, all equipped with SPSS v.22 and SAS v 9.2 for behavioral/treatment data analysis. 3) All computers linked to

Bradley/Hasbro Research Computer server with daily off-site backup. 4) 2 Cambridge Neuropsychological Testing Automated Battery (CANTAB) systems with touchscreens, required peripherals, and a 10-year software license.

**The Pediatric Anxiety Research Center (PARC)** at Bradley Hospital unites Lifespan's strong obsessive compulsive disorder and anxiety programs in a single, remodeled location. The PARC includes leading mental health professionals, researchers in the pursuit of life-changing research, and educators with a passion for patient-centered care. Each of PARC's offered services is designed to bring about vital improvements in the lives of children with obsessive compulsive disorder (OCD) or other forms of anxiety. The Pediatric Anxiety Research Center is ever-expanding, but currently offers: an intensive OCD and anxiety treatment program with two levels of care, services for Tourette Syndrome and other tic disorders and outpatient programs, including the Tic Talk outpatient group

**The Childhood Asthma Research Program** at Hasbro Children's Hospital is a research group that conducts asthma-related studies with the goal of helping children and their families better manage asthma. Examples of studies include (1) Childhood Asthma Research Innovation Program, (2) Project NAPS: Nocturnal Asthma and Performance in School, (3) Physical Activity and Asthma, (4) Pediatric Asthma Disparities, (5) Peer-Administered Asthma Self-Management Intervention in Urban Middle Schools, (6) Controlling Asthma Effectively in School, (7) Emergency Department – Asthma Management Action Plan, (8) A Pilot Study to Improve Sleep Quality in Urban High School Students with Asthma, (9) INTERVENTIONS: Pediatric Food Allergy, (10) Friends, Family, and Food: Interactive Virtual Environments for Children with Food Allergies, and (11) Project FAST - Food Allergy School Transition.

**Kidney Transplant Center:** This transplant center is one of the largest kidney transplant centers in New England region caring for approximately 1,000 kidney transplant recipients and ~70 new transplants per year. This center has a designated infusion center available for clinical studies, which will be used to accommodate patients on study days. The infusion center is located in the out-patient cancer center at the Lifespan Ambulatory Care Center, East Providence, RI. This transplant services is part of the Division of Renal Diseases at Brown Medical School

**Lifespan Dialysis Center:** The main Lifespan dialysis center is located in a 7,500 sq. ft. suite about 0.3 miles from the hospital's main campus. This main center houses 18 patient stations with separate exam rooms and drawing stations. Laboratory: The dialysis units are staffed with specialized nurses with significant experience in accessing fistulas and obtaining blood draws. Dialysis nurses at each center will be responsible for obtaining blood samples for the duration of study. Animal: N/A Office: The Dialysis Center has office space for Dr. Kerns and the nursing staff, a conference room, and additional space available for research staff. Similar space is available in East Providence, RI, within five miles of the main campus.

**COBRE Center for Cancer Research Development (CCRD), Rhode Island Hospital:** The mission of COBRE CCRD at Rhode Island Hospital is to create, interpret and apply new knowledge based on original, collaborative, multidisciplinary laboratory studies of the cellular and molecular pathways leading to carcinoma. Such knowledge will be generated in an environment that fosters career development of promising junior investigators and employs cutting-edge methodology and applications to further our understanding of the cancer process. Basic knowledge gained will be used to design and implement novel diagnostic and treatment protocols to benefit the hospital's patients and the community at large. The COBRE Center provides junior investigators access to the wisdom and experience of senior faculty mentors as well as cutting-edge technologies in biomedical research that were previously unavailable in Rhode Island. The mentoring relationship helps investigators hone their research and investigative skills so that they will ultimately be able to support their research through their own grant awards.

CCRD activities including grant writing workshops, symposia, seminars and biannual advisory committee meetings will be managed and directed by the COBRE CCRD's administrative core. The proteomics core continues to provide the latest technologies and methodologies for analyzing changes in the protein expression profiles that occur when normal cells become cancerous. The goal is to find new markers for early detection and diagnosis. The molecular pathology core continues to build a tissue bank of valuable human tissues and will offer upgraded services for laser capture microdissection, microtissue array preparation, and QPCR. Proteomics and molecular pathology core directors continue to collaborate in the development of new applications for a recently acquired imaging mass spectrometer, applications that we expect to provide new strategies for biomarker discovery and new diagnostic tools for the clinician.

**Orthopaedic Research Laboratory:** The Orthopaedic Research Laboratory has one of the strongest and best funded orthopaedic research laboratories in the nation. Occupying about 25,000 sq. ft. in Rhode Island Hospital (Coro Building, 1 Hoppin St. Providence RI), it is supported by individuals with several NIH R01 grants and an NIH Center for Biomedical Research Excellence (COBRE) for Skeletal Health and Repair. In addition to foundation and industrial support, the funding of the laboratory is over \$20M of current total support. The laboratory has within in, molecular, biochemical, cell biology, morphology and biomechanics expertise and equipment as described below. Many trainees, from the undergraduate, graduate, clinical resident, and postdoctoral fellow levels participate in the laboratories of 10 principal investigators on the same floor. In addition to the basic science laboratories, the Department carries out a substantial translational research program with clinician and basic scientists mentoring a cadre of orthopedic residents, basic scientist and MPH trainees. The learning environment within the department is anchored by several weekly conference series including clinical grand rounds, basic science education, research, and the COBRE. Other relevant conferences on the campus available to trainees include those offered by the Center for Biomedical Engineering at Brown University, which increases multidisciplinary collaborations between investigators.

**COBRE for Skeletal Health and Repair, Rhode Island Hospital:** The COBRE for Skeletal Health and Repair at Rhode Island Hospital enables clinicians, scientists, engineers and biologists to work side-by-side on multidisciplinary research, helping to better understand cartilage and joint health mechanisms and develop strategies for the prevention and treatment of skeletal joint diseases. The goal of COBRE Center is to establish a multi-disciplinary research center focusing on cartilage and joint health, disease mechanisms, and repair strategies. The COBRE aims to initiate and guide cutting edge research projects conducted by promising junior faculties within the scope of Skeletal Health and Repair. In addition, it aims to provide scientific and career mentorship to junior faculty by establishing an Executive Committee that consists of mentors from different research disciplines (clinical, biology, and bioengineering). The PIs interact with the members of the department daily, who have broad expertise in orthopaedic animal models, tissue culture and molecular biology. The projects encompass clinical, biological, and engineering disciplines. This environment gives the PIs access to orthopaedic surgeons and residents who will be recruited for animal surgeries as part of their research obligations. This environment ensures clinicians working side-by-side with basic research scientists, junior investigators with senior investigators, and biologists with bioengineers. This multidisciplinary approach is absolutely necessary to develop translational strategies for prevention and treatment of skeletal and joint diseases. All of the equipment is located on the same floor in the Orthopaedic Research Laboratories in close proximity.

**Lifespan Immunology Research Laboratory:** The Immunology Research Laboratory (IRL) is a 2800 sq ft BL2 lab. It has been in existence since August of 1997 and has grown into a well-known and well respected research specimen processing lab among its peers. It is located in the RISE Building at The Miriam Hospital and functions under the direction of Karen Tashima, MD. The laboratory follows The Miriam Hospital/JCAHO/GCLP/OSHA and CAP standards for laboratory practice and offers a wide range of research specimen processing abilities and storage capabilities to the research community on a fee-for-service basis. With the recruitment of Dr. Angela Caliendo, the laboratory has expanded capabilities to support researchers, including the development of molecular tests that are not commercially available, and modifying current assays to accommodate investigator needs. Consultation on study design with regard to testing methods and results interpretation is also available. Available tests include:

- Nucleic acid extraction for molecular testing and sequencing
- Molecular tests to detect and quantify various infectious pathogens including but not limited to herpes simplex virus and cytomegalovirus testing on genital specimens including tear flow, cervical vaginal lavage specimens, urine, self-collected vaginal swabs, and rectal swabs.
- Quantification of HIV-1 from plasma and genital specimens blood, WBCs, male and female genital specimens, CSF, dried blood spots, and urine
- Detection (and quantification) of HIV-1 DNA from blood, dried blood spots, and genital specimens, and detection of HIV-2 from blood specimens.
- Quantification of HBV, HCV from plasma specimens; and quantification of cytomegalovirus from plasma, genital specimens, CSF, breast milk, dried blood spots.

**Facility:** In this BL2 facility we have (2) biological hoods, (1) shared chemical hood, (14) -70°/-80°C freezers, (4) -20°C freezers, (5) refrigerators, (4) refrigerated centrifuges, (4) ambient centrifuges, 3 incubators, an m2000 sample preparation and real-time amplification system (Abbott Molecular), EZ-1

nucleic acid extraction system (Qiagen and other assorted lab support equipment. We have dedicated rooms for chemical storage, biohazardous waste, liquid nitrogen, and freezers including -20°C to -80°C for specimen storage.). The laboratory has a backup generator and all the refrigerators and freezers are alarmed with 24 hour/7 day monitoring. The liquid nitrogen (LN2) cryotanks and a 230L LN2 tank used for refill are stored in an oxygen monitored and alarmed room for safety. Dry ice is used for shipping and quick-freezing; 165-220lbs are delivered weekly. At present, there are approximately 100,000 specimens stored in both the freezers and the LN tanks, with additional capacity for long term storage of samples including genetic material. There is on site HVAC personnel and a refrigeration company used for freezer repairs.

Experience: The lab has extensive experience with specimen processing of all bodily fluids for the DAIDS network groups, CDC, Walter Reed Military Research Institute and multiple pharmaceutical companies including Boehringer Ingelheim, Gilead, GlaxoSmithKline, Merck, Tibotec, Vertex and 3M. We process samples for Lifespan/Brown researchers in Behavioral Medicine, Pulmonary, Gastroenterology, Oncology and Cardiology Divisions according to research protocols. We process all specimen types include blood, sputum, cerebrospinal fluid (CSF), saliva, stool, and genital secretions. Types of processing include but are not limited to fluid cell counting, reading fluid differentials, gram staining for Bacterial Vaginosis using the Nugent Score for resulting, culturing *Trichomonas vaginalis* and removing Peripheral Blood Mononuclear Cells (PBMC) from blood using different isolation techniques with density gradient medium. The IRL lab has also been involved in assessing and validating new techniques and procedures: examples are dried blood spots (DBS), confidential testing of equipment and strips for FDA approval, OraSure Rapid HIV 1 / 2 testing, the evaluation of a Methicillin Resistant *Staphylococcus Aureus* (MRSA) rapid testing method, and human genetic samples. The laboratory has extensive experience with development and validation of an array of molecular tests for the detection and quantification of pathogens and design and execution of multi-center clinical studies.

In-house Specimen Repository: We have created an Access database for management of the repository. The database is divided by study and is easily accessed. Paper records are kept for backup. The location of the specimen aliquots along with other pertinent specimen information is entered into the database and is quality control checked on a regular basis for accuracy.

Quality Control: The laboratory is regularly reviewed and audited by clinical trials networks and other regulatory authorities to assure quality of work. All study paperwork is kept in study specific binders and filed by visit date for easy access. All regulations are followed to comply with all confidentiality concerns and protocol requirements. Vertical audits have been carried out to ensure that the laboratory personnel are following protocol when processing specimens. The laboratory monitors, evaluates and improves laboratory activities and services by using Deviation and Corrective Action reports. The laboratory follows CAP guidelines for record retention and according to the Lifespan Department of Pathology, Office of Research Administration and study protocol requirements. The laboratory assures the accuracy and reliability of the laboratory facility, equipment, specimens, and results by regularly maintaining equipment and participating in proficiency and quality assurance testing.

**The Immunology Center** provides state-of-the-art care to patients in the community with a team of physicians, nurses, social workers, and psychologists. The Immunology Center employs world-renowned infectious diseases physicians dedicated to helping those with HIV/AIDS live longer, fuller lives. The clinic serves hard-to reach populations and provides care to all patients regardless of their ability to pay for services. The IC provides multidisciplinary care and our team includes onsite social workers, outreach workers, bilingual staff who speak Spanish, Portuguese and Cape Verdean Creole. The IC has strong community relationships and faculty and staff provide on-site HIV prevention and/or treatment services at the following community locations: Rhode Island Department of Corrections (RIDOC); Woonsocket Thundermist Community Health Center; SSTAR Family HealthCare Center in Fall River; MAP Alcohol and Rehabilitation Services; Megaplex Bath House; and SSTAR Substance Abuse Treatment Program.

The Immunology Center consists of a two building complex housing Immunology Physicians and staff for clinical, research and administrative activities in approximately 7,400 square feet. Clinical/research space includes 15 exam rooms, 20 administrative offices, a phlebotomy lab, conference room and six waiting and reception areas. All key personnel have administrative office space separate from the clinical areas and have access to secretarial support. The Miriam Hospital has ample computer capacity and IT support services. Project staff members have access to telephone service, videoconferencing capability, copy services, email

accounts, Internet services, and the Brown University library system. Support services of The Miriam Hospital also include The Miriam Hospital Institutional Review Board (IRB), research administration and finance, human resources, purchasing, telecommunications, building maintenance, and systems support. The Immunology Center offers:

- Comprehensive care for HIV-infected patients
- A program for HIV-infected women that offers case management, clinical trials and gynecological care
- Preconception counseling for HIV-infected women and men, including serodiscordant couples, as well as specialized care of HIV-infected pregnant women in collaboration with their obstetricians
- The country's first HIV and menopause clinic
- An HIV program for adolescents that offers intensive care and long-term support
- One of the country's first HIV/viral hepatitis co-infection treatment programs
- Infectious diseases and HIV-related clinical trials sponsored by the federal government and pharmaceutical companies
- Free active outreach care and HIV/STD prevention for substance abusers (particularly heroin and cocaine needle users), offered in collaboration with AIDS Care Ocean State
- HIV care that is linked to the community at the state prison and substance abuse treatment sites
- Participation in four federally funded HIV prevention programs for adolescents, high-risk women, and men and women leaving prison

The Immunology Center is a major component of the Lifespan/Tufts/Brown Center for AIDS Research (CFAR).

**The Clinical Research Site:** The IC is home to the Clinical Research Site (CRS) of the TMH, co-located in the same building to facilitate access and participation. The CRS team consists of consists of Dr. Tashima (CRS Leader, CSC faculty), a study coordinator, and staff members including research nurses, data manager, regulatory coordinator, and research assistant. The focus of the CRS continues to be engaging women, minorities and other underserved populations in clinical trials. During the current funding period (12/2013 - 11/2020), the TMH CRS is enrolling into ACTG studies involving interventional, observational and genomics studies. Currently, there are 13 active ACTG studies and 12 pharmaceutical studies enrolling patients. The CRS has consistently met the DAIDS standard of maintaining an average monthly census of at least 20 participants on interventional trials and the ACTG standard of maintaining an average monthly census of at least 40 participants on interventional and observational studies.

**The Sexually Transmitted Disease Clinic.** The Miriam Hospital STD Clinic will serve as one recruitment site for Aim 1. The STD Clinic is co-located with the Immunology Center and the clinical PrEP Program. Thus, the Clinic has access to the clinical resources of the Immunology Center. 26 The STD Clinic is an urban walk-in clinic that provides safety-net services for the diagnosis and management of STDs. Clinic staff also include a physician's assistant (PA), a nurse, a clinic manager, and a database specialist. It is the only STD clinic in RI with patients also referred from western Connecticut and southern Massachusetts. An average of 150-200 patients are seen in the clinic per month. The patient population is racially and ethnically diverse. Individuals are referred from community-based organizations and clinics, the Rhode Island Department of Health, and other medical centers. In 2014, 30% of all patients were MSM. The clinic had a 1.0% seroprevalence of HIV among the general clinic population and 2.2% among MSM; 15.5% of individuals tested positive for at least one STD. The STD Clinic and the larger Immunology Center refer high-risk HIV negative patients directly to the onsite PrEP Program for further evaluation All individuals who present for testing at the STD Clinic currently undergo a demographic and behavioral assessment as mandated by the Department of Health for surveillance purposes. These data include age, gender, race/ethnicity, sexual orientation, sexual behaviors, drug use, and other risk factors related to HIV/STD infections. Individuals are also asked how they were referred to our site. This information is used to inform personalized education and behavioral counseling. Individuals are routinely tested for HIV (antibody test), hepatitis C (antibody test), syphilis (serum), gonorrhea, and chlamydia. Gonorrhea and chlamydia testing is performed via nucleic acid amplification testing (NAAT) of the urine on all individuals. MSM also have testing of their oropharynx and rectum by NAAT. Individuals are also screened for acute HIV infection by clinical signs and symptoms. If there is concern for acute infection, an HIV viral load is obtained. Other laboratory testing is available on a case-by-case basis (e.g., herpes simplex virus 1/2, hepatitis B).

**Pre-Exposure Prophylaxis (PrEP) Program.** The clinical PrEP Program at The Miriam Hospital is co-located with the Immunology Center and the STD Clinic, with access to the resources of the Immunology Center. The PrEP Program was founded by Dr. Chan in 2013 to address the increasing trend in HIV among MSM in RI; more than 50% of all new HIV diagnoses in RI are MSM. As of July 2015, 102 individuals had been prescribed PrEP (M age = 34 years; 71% White/Caucasian, 22% Hispanic or Latino; 93% MSM). Of the MSM, 30% were in serodiscordant relationships, and 22% reported recent anal sex with a HIV+ man. The PrEP Program follows current CDC guidelines; thus, on initiation of PrEP, individuals are evaluated for behavioral risk factors and

laboratory testing is performed for HIV antibodies, a viral load (if acute HIV is suspected), other STDs, renal function, and hepatitis B status. Individuals are followed-up as recommended.

**The Center for AIDS Research (CFAR)** The Providence/ Boston Center for AIDS Research (CFAR) is a joint research effort between Brown University/Lifespan, Boston University/Boston Medical Center and Tufts University/Tufts Medical Center. The CFAR is part of a national program begun by the National Institutes of Health in 1988. There are currently 20 Centers for AIDS Research (CFARs) located at academic medical centers throughout the U.S. The Providence/Boston CFAR has brought together all senior AIDS investigators at the Tufts, Boston, and Brown Universities and their affiliated hospitals in a user-friendly structure which has been successful in supporting on-going research among active AIDS investigators and in stimulating new AIDS research by young investigators and by others who had not previously been involved in this research area. Besides the extensive efforts in Southeastern New England, the leadership has expanded the scope of international studies through the training of international collaborators and collaborative research at international sites. CFAR Core Services are available to support HIV/AIDS research to all affiliated Boston University, Tufts University, and Brown University faculty members who hold the rank of assistant professor or greater. The full range of research disciplines including behavioral science, basic science, clinical research, prevention science, and international research are supported by the CFAR.

The CFAR laboratory is located at The Miriam Hospital in the recently renovated space at the CFAR building in Providence RI. It is approximately 2500 square feet (about 1250 square feet for each lab), with an additional 850 square feet of shared space which includes freezer rooms, a chemical storage and biohazardous waste room, storage room for supplies and archived material, liquid nitrogen tank room with its own ventilation system, a utility room and office space. It consists of six Biosafety Level 2 (BSL2) laboratories; one for specimen processing with a separate designated shipping area, two for molecular biology work, one microbiological work, one clean room for PCR amplification and one Post-PCR room for data visualization and analysis. The laboratory adheres to good clinical laboratory practices (GCLP) guidelines and has developed a quality management system. The laboratory is equipped to perform molecular, biochemical, immunological and serological assays and microbiology. For HIV drug resistance testing the laboratory participates in a yearly European Network for Virologic Evaluation (ENVA) HIV Drug Resistance External Quality Assessment Program provided by Quality Control for Molecular Diagnostics (Scotland, UK <http://www.qcmd.org/>). Personnel are trained to handle human biological materials and employ strict precautions that reduce risk of accidental exposure and are IATA certified in shipping.

The laboratory has a quality management system that is followed based on GCLP guidelines. Supported studies include NIH, CDC, ACTG, pharmaceutical trials and other private studies conducted by CFAR investigators. The laboratory has extensive experience with a variety of specimen types including blood, cervical/vaginal lavages, cerebrospinal fluid, menstrual blood, saliva, semen, stool, urine and vaginal secretions collected by various methods. Quality assurance testing is performed on various specimen types to check for semen contamination using the ABA card p30 rapid test. The laboratory is experienced with procedures such as specimen processing, fluid cell counting, reading fluid differentials, gram staining for bacterial vaginosis using the Nugent Score, trichomonas cultures using both the Diamond Media and In Pouch method and peripheral blood mononuclear cells (PBMC) processing using different isolation techniques with density gradient medium. All specimens are received into the laboratory with specimen requisitions which are used to assist in the documentation, processing, shipping and/or storage. Specimens are given a participant ID so that the patient's identity always remains confidential. The laboratory manages a large in-house repository of specimens with a newly developed Access computer database. The laboratory also uses the Laboratory Data Management System (LDMS) through Frontier Science that is required by the ACTG/HVTN networks, which is a comprehensive program for managing specimens from receipt to storage and shipment.

The Access database used for the laboratory's repository is divided up by study. Paper records are kept for backup. The location of the specimen aliquots along with other pertinent specimen information is entered into the database and it is quality control checked on a regular basis for errors. From here, queries can be made to review repository specimens available for testing and shipment with ease. The laboratory has periodic inspections and auditing done by different networks and regulating authorities to assure the quality of work. All study paperwork is kept in study specific binders and filed by visit date for easy access. All regulations are followed to comply with all confidentiality concerns and protocol requirements. Vertical audits have been done to ensure that the laboratory personnel are following protocol when processing specimens. The laboratory monitors, evaluates and improves laboratory activities and services by using Deviation and Corrective Action reports. The laboratory follows the College of American Pathologists (CAP) guidelines for record retention and

the Lifespan Department of Pathology, with added recognition of the study protocol requirements. Participation in a Point of Care Testing Program, operating under Lifespan's Pathology Laboratory's CLIA License for Point of Care Testing and the CAP Survey proficiency program for Rapid HIV testing, is mandatory and necessary for quality assurance. The laboratory strives to assure the accuracy and reliability of the laboratory facility, equipment, specimens and results by regularly maintaining equipment, participating in proficiency and quality assurance testing such as CAP surveys and a PBMC processing quality assurance program. The laboratory closely and actively collaborates with Core Centers including The Center for Genomics and Proteomics at Brown University and The Rhode Island Genomics and Sequencing Center (RIGSC) at The University of Rhode Island, which are both within driving distance from the Laboratory.

**The Departments of Emergency Medicine (EM):** Brown University EM is one of the largest departments in the country, providing clinical services to greater than 260,000 patients per year; the department is staffed by 109 faculty, 7 PhDs, 48 emergency medicine residents, and 11 fellows. The department supports a well-established research program, with greater than \$5 million in annual external grant funding. The Emergency Medicine Research Laboratory activities are focused on bioengineering and biophotonics projects which are translationally important to the care of Emergency Medicine patients. The Division of Emergency Neurosciences (DEN) within the Department of EM is a multidisciplinary consortium to study traumatic brain injury, stroke, seizure, and hydrocephalus. The DEN is composed of 40 cross discipline faculty from Emergency Medicine, Neurosurgery, Critical Care, Orthopaedics, Neurology, and Diagnostic Imaging. DEN supports industry, foundation, and federally funded Phase I, II, and III clinical trials, with fulltime research support and in-house clinical trial coverage.

**Sex and Gender in Emergency Medicine.** In 2010, the department of emergency medicine at The Warren Alpert Medical School of Brown University established a division of women's health in emergency care (WHEC) and a two-year WHEC fellowship to train a new generation of physicians in sex and gender-specific emergency medicine. The division includes Brown emergency medicine faculty members and a multidisciplinary panel of advisors from the medical school and other institutions around the country. In 2014, WHEC updated its name to the division of sex and gender in emergency medicine (SGEM) to align itself with growing research in sex differences and the national emphasis on examining the health of women and men to help understand diseases. SGEM's mission is to establish educational and research endeavors that promote sex-and-gender-specific medicine and women's health as it relates to the practice of emergency medicine.

**The Division of Imaging Research** at Rhode Island Hospital was established in 1990 and has successfully completed both federally-funded and industry-sponsored research trials. The division has participated in 10 federally-funded cancer imaging trials through the National Cancer Institute (NCI) and ECOG-ACRIN. These trials include screening studies and studies looking at the efficacy of various imaging modalities. The division has participated in studies with pharmaceutical companies on phase I, II, and III trials. These studies include both diagnostic and cancer treatment drugs. We have also worked with various device manufacturers that are seeking pre-market and post-market Food and Drug Administration approval for medical devices. In addition, we have participated in several blood biomarker studies. We have extensive experience working with various clinical research organizations and are adept with both paper and electronic data submission. The division is academically affiliated with the Warren Alpert Medical School of Brown University. Also, the physicians in our department that serve as study investigators have a long standing working relationship with all the physicians in our facility. These relationships strengthen our enrollment efforts and provide the Division of Imaging Research with the unique opportunity to offer various patient populations in the community a broad range of research trials.

**Hospital-Imaging Research and Education Service (HI-RES):** The hospital-imaging research and education service (HI-RES) was established in 2014 as a core service supporting the growth of imaging research and education among hospital-based staff. HI-RES is a joint-venture with the Norman Prince Neurosciences Institute (NPNI) and the departments of neurology, neurosurgery, psychiatry and diagnostic imaging at The Warren Alpert Medical School of Brown University. HI-RES serves the Lifespan (Rhode Island, The Miriam, Hasbro Children's, Bradley and Newport hospitals) and Care New England (Butler, Women and Infants, and Kent County hospitals) healthcare systems as well as the Providence VA Medical Center. HI-RES has two image analysis and education centers, one at Rhode Island Hospital and the other at Butler Hospital. The Rhode Island Hospital site features advanced computing for image analysis, an image processing server, conference room and three offices. The Butler Hospital site consists of two room that house eight computers equipped for image analysis. HI-RES also utilizes Brown University's high performance computing center (HPC).

HI-RES has a dual mission:

- Research mission: To foster collaborative imaging research both in/within stakeholder departments and also to foster collaborative links to Brown University campus-based researchers. This has the potential to include trainees interested in hands-on research projects as well as hospital-based faculty.
- Education mission: To bolster the interdisciplinary education of hospital-based trainees in the use of imaging, particularly neuroimaging, to advance the understanding of the biological basis of neurodevelopmental disorders. This will include didactic sessions, journal clubs and hands-on sessions with trainees, including medical residents and PhD- trainees.

**Department of Diagnostic Imaging:** Within RIH, the Department of Diagnostic Imaging (DDI) is staffed by sixty board-certified diagnostic radiologists who review 450,000 thousand cases per year, perform over 2000 image guided procedures, and supervise the training of 34 radiology residents/fellows. Dedicated physics staff calibrate and maintain the diagnostic imaging equipment and provide radiation safety services. All pertinent data, systems, security, and tech personnel are accessible to the proposed project. The proposed research program will be conducted primarily within the 3D Lab, a state-of-the-art 1800 square foot dry lab facility dedicated to medical image analysis. This collaborative space provides computational research workstations within the hospital. Scientific software, design, and programming tools include: COMSOL Multiphysics, ImageJ, Slicer3D, Matlab, SAS, SPSS, AutoCAD, ITK, VTK, Python, VisualStudio, Xcode, Office, and the Adobe Creative Suite.

**The Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS)** project is an ongoing clinical research study involving the integration of research assessment methods into routine clinical practice. Nearly 4,000 psychiatric outpatients presenting for treatment in a hospital-affiliated, community-based, practice setting have been comprehensively evaluated with semi-structured diagnostic interviews including the Structured Clinical Interview (SCID) for Axis I disorders and Structured Interview for DSMV-IV Personality (SIDP) for Axis II disorders. Information on childhood trauma, family history of psychiatric disorders, psychosocial functioning, and demographic features has been obtained as well.

- Quality and Outcome of Treatment in the Partial Hospital Program. Patients complete measures of depression, anxiety, and anger on a daily basis. An assessment of symptoms, quality of life, coping ability, overall sense of well-being, and psychosocial functioning is completed at admission and discharge. Patient satisfaction is assessed at intake and at the completion of treatment. Recent analyses have examined the predictors of premature drop-out. Future analyses will examine the speed and predictors of response.
- Development of New Assessment Tools. A primary focus of this project is the development and investigation of newly constructed measures for clinician ratings of symptom severity/impairment and self-report questionnaires for patients. Projects have included validation of a questionnaire designed to assess DSM-IV major depressive disorder (Diagnostic Inventory for Depression, DID), and a questionnaire that screens for a broader compliment of DSM-IV diagnoses (the Psychiatric Diagnostic Screening Questionnaire, PDSQ).
- Bariatric Surgery Program. MIDAS evaluates prospective surgical candidates with comprehensive semi-structured interviews for DSM-IV Axis I and Axis II disorders, as well as a supplemental interview module specifically focused on issues related to bariatric surgery. The initial goals of the program are to determine the percentage of patients who are not cleared for surgery due to psychiatric reasons and what those reasons are. During the past seven years more than 3,500 patients have been evaluated.

**Bradley Hospital Sleep and Chronobiology Research Laboratory (Sleep Lab):** The Sleep Lab is located in two adjacent buildings on the campus of Butler Hospital on the East Side of Providence (200 and 300 Duncan Drive, Providence, RI). The Sleep Lab shares the campus with the in- and out-patient psychiatric services buildings of Butler Hospital and several other tenants. This setting is pleasant, with trees, lawns, ample parking, and a congenial ambience for in-lab assessments.

The main laboratory building is a renovated structure that offers approximately 6,000 sq ft of laboratory, office, and storage space. A Sleep/Chronobiology laboratory is located on the ground floor. Construction of this 4-bedroom laboratory space took into consideration all special building requirements needed for chronobiological and sleep studies, including lighting, heating, ventilation, air conditioning, noise control, and the comfort and safety of study participants. Each bedroom in the laboratory is equipped for digital polysomnographic recordings and visual (with remote pan, zoom and tilt controls; video monitoring is functional in normal light, dim light, and infrared (IR) light available in each bedroom), audio, and ambient temperature monitoring;

controls in the tech monitoring area provide centralized control of lighting levels and ambient temperature. Digital data acquisition systems (Grass-Telefactor TWin) provide acquisition of over 40 physiological (or transduced) signals from each bedroom with simultaneous video recording. Two small centrifuge in the technical area is available for immediate preparation of saliva samples. A special interface between the floors dampens noise carry through from the floor above the sleeping rooms. The technical staff can communicate with each bedroom over an intercom system, and participant's vocalizations are picked up through ceiling mounted microphones. An audio/video door annunciator links the technical staff to the Sleep Lab's main entrance so that technical staff can monitor and respond to visitors to the main building without having to leave the central technical area. Also located in the ground floor lab space is a small examination room, storage area, and a -20°C freezer for immediate storage of biological samples.

In terms of a research participant's experience in the lab, each bedroom has a bed (single with cranks to raise head, feet, or knees), a small desk with personal computer for performance testing, closet, clothing bins, bedside table, and television monitor. For most protocols, participants spend their "free" time in the common area/play room, where they take part in group activities. Principal features of the play room are a "white board," a games closet (stocked with a large assortment of board games), a crafts cabinet (stocked with many types of craft activities), and a large video monitor. The latter is used for family style movie-watching sessions and to play the tai chi video for family-style stretching exercises. A fully equipped kitchen located on the floor above the lab allows for 24-hour meal preparation. This laboratory floor of the building is without windows, and lighting is under control of the supervisory technical staff at all times. Upper stories of the main Sleep Lab building include offices (described) below, a conference room, and two attic storage areas. The second building of the Sleep Lab, the "Annex," also has offices (see below) and includes a large room that is used as a classroom for the summer apprenticeship. In addition, a second -20°C freezer and a -80°C freezer are located in that building.

**Computers** The Sleep Lab's local area network operates via a Pentium-class server housed offsite in the secure server facility of Lifespan Computer Information Services (CIS). A high-speed T1 line connects the laboratory buildings to the offsite server and enables internet access and access to the Lifespan intranet and Brown University internet services (including direct access to Brown's extensive electronic library holdings and to Brown's library support services). Lifespan CIS supervises daily backup of server data and provides 24-hour/7-day technical support for the server and all computers and printers on the local area network. The laboratory and offices in the main laboratory building are equipped with Pentium-class personal computers with Windows operating systems for EEG data collection, Macintosh personal computers for staff, high-speed laser printers networked to computers, a printer/copier/fax machine, and a large format poster printer. The Macintosh desktop computers are used for word processing, forms development, data entry, data analysis, data storage, and so forth; these Macintosh computers are linked to a central back-up server for weekly backup of desktops. Four of the Pentium-based PCs are dedicated to the PSG recording systems, and data are backed up to an onsite-server daily; this server is backed up (mirrored) daily to an off-site server at the Lifespan facility. Four PCs support computerized neurobehavioral data collection in participant bedrooms, with results written directly to the Lifespan server. Another computer is used for actigraph interface. VitaScore software for scoring digital sleep records on is located on two PCs and the TWin work stations. One Macintosh computer is used as a server for iPod-based data collection. The laboratory has 8 iPods for in-lab data collection connected to the server via a wireless network.

## **LIFESPAN COMPUTER AND INFORMATION AND RESOURCES**

**Lifespan Hospital System Data and Computational Resources Network:** The Lifespan Data and Computational Resources Network is part of the Biostatistics Core in the Lifespan Hospital System, RI. Lifespan is a comprehensive, integrated, academic health system affiliated with the Alpert Medical School of Brown University. The Lifespan Hospital System includes The Miriam Hospital, Rhode Island Hospital (including the pediatric division, Hasbro Children's Hospital), Bradley Hospital, Newport Hospital, and Gateway Healthcare. The network includes experts in data management, statistics/biostatistics, bioinformatics, computer science, and other computationally- or data-minded individuals spread throughout the Lifespan Hospital System and surrounding academic institutions. The network's mission is to support the research community across a broad range of data and computational specialties, as well as facilitate collaboration and logistics, provide advocacy and peer-mentoring, and assist in personnel and asset management.

**Lifespan Computing & Information Services:** All hospital-based users have access to the Internet and E-mail resources provided by Lifespan, the parent corporation of Rhode Island Hospital. Investigators have off-

site access to the network through use of a Virtual Private Network (VPN) connection. Rhode Island Hospital also owns and operates an extensive network of mainframes, minicomputers, and microcomputers. These systems are made available to the University community through an advanced broadband, coaxial local area network, which features data transfer up to 2 MBPS. The Information Technology 24/7 Support Center at Rhode Island Hospital sets up all new computers, repairs existing computers, and manages secure storage of research data. Secure access has to be granted before research staff can access shared files. Hard drive data are backed up daily, and are HIPAA compliant, password-protected, and limited to her use.

**Electronic Health Record Systems:** The Warren Alpert Medical School is affiliated with seven area hospitals - all within a fifteen-minute drive of the Brown campus - that serve one and a half million people of diverse backgrounds and socioeconomic status. Emma Pendleton Bradley Hospital, Rhode Island Hospital and its Hasbro Children's Hospital, and The Miriam Hospital are part of Lifespan, Rhode Island's first health system, which transitioned to an Epic-based EHR in 2015. Lifespan's Legacy Data Warehouse archives clinical and patient financial data from retired EHR systems, including Siemens INVISION and the MEDHOST Emergency Department Information System, which were in use until March 2015. Butler Hospital, Memorial Hospital of Rhode Island, and Women & Infants Hospital of Rhode Island are part of the Care New England Health System, which have been using multiple EHR systems in different settings and are in the process of transitioning to the Epic EHR, initially for outpatient care.

The hospitals use a single electronic health record system (Epic), guaranteeing seamless communication at all levels of the institution. The system provides real-time information regarding patient age, complaint, and other demographics from the time that a patient presents to the emergency department. Numerous Epic workstations, both fixed and portable, are located throughout the emergency department, the Center for Medical Imaging, the Operating Suite, the Post-Anesthesia Care Unit and the surgical wards, as well as within the Pediatric Emergency Medicine office suite and in the Emergency Medicine Research Assistants' office. Project research assistants use tablet computers to securely screen potential patients and to complete baseline measures for those enrolled. This blend of information technologies permits effective and secure data collection, transmission, storage, and analysis. These resources provide the research team with the facilities necessary for research development, research implementation, analysis, and preparation of data reports and manuscripts.

**REDCap Software:** Hosted at Lifespan's Department of Information Services, REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. REDCap is implemented at Lifespan using a 2 server architecture housed at a secure Data Center location dedicated to Information Services and manned 24x7x365. One server is public facing, supplying the web portion and giving users access to the REDCap URL. The other server is inside the Lifespan network and has all the collection data. This architecture was designed by network engineering and approved by IS Security. Both servers are backed up daily and monitored for hardware failures. Spare parts are kept on site with more severe hardware failures managed with a 4 hour turnaround time through a contract with SMS.

**URSA and RI-REd:** Through a partnership between Lifespan and Care New England, Rhode Island Research and Education (RI-REd) was established as a shared infrastructure for the secure collection, management, and analysis of electronic health data for research and educational purposes. As a functional proof-of-concept, RI-REd has hosted REDCap (Research Electronic Data Capture) for more than a year in a cloud-based environment. Brown University recently joined the partnership and is working with the partner institutions to migrate RI-REd into the "Stronghold" computing environment at Brown that adopts HIPAA security measures. This effort is being coordinated by BCBI in close collaboration with information services, compliance programs, and research offices at Brown, Lifespan, and Care New England. In addition to REDCap, RI-REd will house other research systems such as i2b2 (Informatics for Integrating Biology & the Bedside). The URSA (Unified Research data Sharing and Access) initiative provides a formal framework for requesting and using data from these systems, as well as other sources including EHR systems at Lifespan and Care New England, for Brown-affiliated investigators.

### **LIFESPAN SUPPORT FOR INVESTIGATOR INITIATED CLINICAL TRIALS**

**The Ocean State Clinical Coordinating Center (OSCC)** facilitates the investigation of new medical interventions and diagnostic solutions. We specialize in designing and implementing clinical trials of novel

agents, diagnostics and devices to confront medical issues related to critical care, infectious diseases and biological defense. The OSCCC is a partnership of experts in critical care, infectious disease and pulmonary medicine who provide both administrative and clinical support for the hundreds of study sites involved in our trials. The OSCCC goal is to generate consistent interpretation of enrollment criteria and to assure the accurate execution of clinical protocols. We specialize in designing and implementing clinical trials to confront infectious diseases and biological defense. The office is located within minutes of Rhode Island Hospital, which allows the OSCCC staff immediate access to resources only an academic medical center can offer. The center enables study sites to contact OSCCC physicians 24 hours a day, 365 days a year. An OSCCC physician approves every clinical trial subject resulting in the highest level of enrollment consistency and protocol execution accuracy.

**Biostatistics Consultation Services and Data Management:** The Lifespan Biostatistics Core (located at RIH campus) provides centralized biostatistics consultation for researchers in the Lifespan hospital group. It staffs 2 PhDs, one Masters Biostatistician, and hosts an externship. Members have more than 200 combined peer-review publications. Researchers are encouraged to involve the core in all phases of their projects from conceptualization through dissemination. The core either supplies direct support or assists in resource acquisition through its Data and Computational Resources Network. As a central resource for a vast array of research subjects, it serves as a hub for collaboration and cross pollination of ideas, techniques, and capabilities. Specific biostatistics services may include: • Experimental design for study development • Data management • Power analysis • Descriptive and inferential statistical analyses of study results • Technical writing of study methods, analysis, and results • Data queries and interim analysis • Customized reports and data displays Consultations and services are offered on a fee-for-service basis, with opportunity to form formal collaborative efforts in co-investigator roles for percent effort. The Core focuses on maximizing the validity of scientific analysis, which sandwiches methodology and statistical analysis between conceptualization and interpretation. The intimate dependency of "analysis" on prior knowledge, logic, methodology, and statistics is a focus of the core. Researchers of all academic and funding levels are encouraged to involve biostatistics as early in their process as possible, including brain-storming sessions on theory development, hypothesis generation, methodology, measurement selection and assessment, and ultimately data analysis and dissemination. The Core also serves as a point of intersection for hundreds of researchers, having facilitated the creation of numerous new collaborations between researchers who may not have otherwise crossed paths. The Core is directed by Jason T. Machan, Ph.D.

**Lifespan Clinical Research Center and Affiliated Resources (LCRC):** The LCRC is directly overseen by the Senior Vice President and Chief Research Officer for the Lifespan Hospital System. Bharat Ramratnam, an experienced clinical investigator, serves as Medical Director and supervises LCRC activities. The LCRC serves as an institutional resource to support investigators in the conduct of clinical research. Through the LCRC, centralized human and physical resources are provided, to facilitate the expert conduct of clinical research across departments and medical specialties. The LCRC provides a range of services including support for study design and analysis, research nursing support and medical oversight (as needed) for study conduct, and both project management and regulatory affairs support. The LCRC is available to investigators throughout the Lifespan hospital system as well as those affiliated with any of our collaborative partner institutions. LCRC staff includes Research Nurses, Project Directors, Research Assistants, Laboratory Technicians, and Research Administrators.

The LCRC maintains two outpatient clinical research units (CRU's), one located in the Coro Building for the Rhode Island Hospital campus, and the other located in the RISE Building, for The Miriam Hospital Campus. These two units may be used to perform a wide range of outpatient clinical research, including Phase I-III clinical trials and infusion studies. The LCRC has established its administrative offices in the Coro Center, a centrally located 270,000 sq. ft. building complex that is home to most of the research laboratories for the Lifespan Hospital system. Within this 3,000 sq. ft. LCRC suite, there are five examination rooms available for investigators use to conduct clinical research procedures. The other CRU is located at The Miriam Hospital, available to directly support investigators and study participants at this location. The Miriam Hospital CRU includes three additional examination rooms. Exam rooms at both locations are fully equipped with examination tables and standard medical diagnostic equipment. As noted above, the LCRC also maintains ready and stable access to several infusion beds, located within a newly constructed infusion suite at The Miriam Hospital, for higher-risk and medically-intensive clinical trials. In addition, the Lifespan Oncology Clinical Research program (LOCR) spans across both Rhode Island and The Miriam Hospitals with access to more than twelve exam rooms. This program includes 10 staff (including Research Nurses and Project Coordinators)

that provides a full-range of clinical trial support services for investigators in medical oncology and hematology, radiation oncology, surgical oncology, neuro-oncology and pediatric oncology.

**Biologic Specimen Processing Laboratory and BioBank.** The Specimen Processing Laboratory (SPL) is a 2800 sq. ft. BL2 lab composed of the Immunology and Microbiology Research Labs. It has been in existence since August of 1997 and has grown into a well-known and well-respected research specimen processing lab among its peers. It is located on the first floor of the RISE Building at The Miriam Hospital and functions under the direction of Karen Tashima, MD. The laboratory follows The Miriam Hospital/JCAHO/GCLP/OSHA and CAP standards for laboratory practice and offers a wide range of research specimen processing abilities and storage capabilities to the research community on a fee-for-service basis. The SPL facility (BL2 rated) contains (2) biological hoods, (1) shared chemical hood, (14) -70°/-80°C freezers, (4) -20°C freezers, (5) refrigerators, (4) refrigerated centrifuges, (4) ambient centrifuges. We have dedicated rooms for chemical storage, biohazardous waste, liquid nitrogen, and freezers including -20°C to - 80°C storage. The laboratory has a backup generator and all the refrigerators and freezers are alarmed with 24-hour/7 day monitoring. The liquid nitrogen (LN2) cryotanks and a 230L LN2 tank used for refill are stored in an oxygen monitored and alarmed room for safety. Dry ice is used for shipping and quick-freezing; 165-220 lbs. are delivered weekly. At present, there are approximately 100,000 specimens stored in both the freezers and the LN tanks, with additional capacity for long-term storage of samples including genetic material. There is on site HVAC personnel and a refrigeration company used for freezer repairs. In-house Specimen Repository: An extensive specimen repository bank is maintained and an Access database is used for management of the repository. The database is divided by study and is easily accessed. Paper records are kept for backup. The location of the specimen aliquots along with other pertinent specimen information is entered into the database and is quality control checked on a regular basis for accuracy

**Quality Control** The laboratory is regularly reviewed and audited by clinical trials networks and other regulatory authorities to assure quality of work. All study paperwork is kept in study specific binders and filed by visit date for easy access. All regulations are followed to comply with all confidentiality concerns and protocol requirements. Vertical audits are carried out to ensure that the laboratory personnel are following protocol when processing specimens. The laboratory monitors, evaluates and improves laboratory activities and services by using Deviation and Corrective Action reports. The laboratory follows CAP guidelines for record retention and according to the Lifespan Department of Pathology, Office of Research Administration and study protocol requirements. The laboratory assures the accuracy and reliability of the laboratory facility, equipment, specimens, and results by regularly maintaining equipment and participating in proficiency and quality assurance testing.

### **LIFESPAN CORE RESEARCH FACILITIES**

**The Coro West/East complex** is a large facility owned by Rhode Island Hospital in the Providence Knowledge District. Current occupants of this complex include the COBRE for Cancer Research Development (Administrative and Proteomics Cores), the RIH Core Research Labs (CRL), Department of Orthopedics research labs, the COBRE for Skeletal Health and Repair and the Cardiovascular Research Center. The Coro Complex is surrounded by other basic research centers owned by Rhode Island Hospital (the Liver Research Center, the Division of Endocrinology), Brown University (Molecular Medicine Institute and COBRE for Signaling in Cancer), Miriam Hospital (Weight Loss and Diabetes Center) and Woman and Infants Hospital (Kilguss Neonatal Research Center and COBRE for Perinatal Biology) and the Institute for Immunology and Informatics.

**Medical Simulation Center:** Medical simulation is the set-up, monitoring and review of a controlled medical event, designed to educate health care providers and broaden their experience with critical situations. Because simulations are completely staged, participants are able to make mistakes a Medical simulation technology allows for realistic clinical scenarios using life-sized computerized patient manikins that are able to respond in real-time to a variety of clinical interventions and pharmacologic agents. This type of technology offers medical educators a new way to control situational learning. The goal of the Rhode Island Hospital Medical Simulation Center is to actualize this potential and create a learning environment which fosters the development of superior clinical skills without risk to patients. The computer-driven manikins range from \$30,000 to \$200,000 and are capable of verbal communication, accurate representation of common physical exam findings (airway compromise, lung and cardiac sounds, pulses etc), and physiologic responses to drug and treatment interventions. Realistic representations of actual treatment settings allow simulation participants to suspend

disbelief and immerse themselves in the training exercise. Participants involved in the simulation may include physicians, nurses, allied health care personnel or multidisciplinary teams.

**Animal:** The animal care facilities operate in full compliance with the OLAW/PHS policy on the Humane Care and use of Laboratory Animals and the USDA Animal Welfare act. The Hospital's NIH Assurance number is A-3922- 01 and the USDA Registration number is 15-R-002. Laboratory animal care and use programs at the Hospital are accredited by the Association for the Assessment and Accreditation of Laboratory Animal care, International, file number 205. The facility includes procedure areas, surgical facilities, and sections to accommodate animals on biohazardous and conventional protocols. Veterinary care at the facility is under the supervision of Drs. Lara Helwig, DVM, Tiffany Borjeson, DVM, and Jessica Johnston DVM. The services of Drs. Helwig, Borjeson, and Johnston are provided through an agreement with Brown University's Division of Biology and Medicine. The veterinarians have access to the Hospital's corporate management and have appropriate authority to ensure the provision of adequate veterinary care in the animal facilities.

**Core Research Laboratories** offer critical technical services including: 1) Digital Imaging/Image Analysis & Confocal Microscopy, 2) Flow Cytometry, 3) Transmission Electron Microscopy, 4) Scanning Electron Microscopy with X-ray (Elemental) Microanalysis capability, 5) Histology/Histochemistry, 6) DNA Sequence Analysis, and 7) Gel Scan Analysis. The core is also used for research training and education.

**Proteomics Core within the COBRE for Cancer Research Development:** The mission of this Center of Biomedical Research Excellence (COBRE) is to develop and support investigators, particularly those engaged in cancer research, by providing expertise, equipment, and mentoring. The Proteomics Core provides cutting-edge biotechnology for analyzing how proteins change with malignant transformation, and facilities to enable discovery of markers that could be used for early detection and diagnosis of cancer. Equipment includes: Bruker MALDI-Imaging Mass Spectrometer and ImagePrep matrix sprayer for direct analysis of proteins, lipids, and modified proteins in tissue; Bruker suspension array; AB SCIEX QSTAR XL Mass spectrometer for protein structural and conformational analyses; Dionex UltiMate 3000 Nano HPLC; HPLC; Thermo Scientific Q Exactive Benchtop LC-MS/MS; Agilent BioAnalyzer 2100 for sizing and quantifying RNA, DNA, proteins, and cells; Bioinformatics software for mass spectrometry (ProteoIQ, HD Examiner DXMS, MASCOT search engine); ProBot LC/MALDI spotter; Thermo Scientific NanoDrop 2000, Bioinformatics HP HPZ 800 workstation, and a Robotic Fluidics station. In addition, technical assistance is available for gel analysis and imaging, and sample extraction, preparation and analysis with the available resources.

**Molecular Pathology Core** within the COBRE for Cancer Research Development: This facility is directed and maintained by the Department of Pathology at Lifespan and the COBRE Center for Cancer Research Development. Equipment and services include: Laser Capture Microdissection, Quantitative Real-Time PCR, Tissue Microarray production, human tumor and tissue banking, automated immunohistochemical staining and in situ hybridization (Ventana Discovery System), data and image analysis. In addition, small-scale tissue processing and analyses are available.

**Multiplex/Translational Research Laboratory:** This laboratory was established to perform high through-put protein and nucleic acid based assays using human tissue and biological fluid samples. However, the same platforms are also used to process large numbers of samples from experimental models used in preclinical studies. Unique equipment includes: bar-coding instrumentation (HHP) for storage and retrieval of samples, Bio-Plex 200 and Mag-Pix machines for multiplex ELISAs and gene expression studies, multiplex RNA analysis, robotic liquid handlers, RNA and DNA automated extraction equipment, multi-sample tissue homogenizers, stereology equipment and software, a Roche 480 qPCR machine, safety hoods for human tissue dissection, and tissue choppers for generating organotypic slice cultures. In addition, equipment and expertise are available for performing 3-D stereology, rodent neurobehavioral phenotyping (rotarod; Morris Water Maze), and ultracentrifugation.

**The Julia and Dr. Vincent Zecchino Orthopaedic Research Suite** consists of Cell and Molecular Biology Laboratory (Director: Dr. Qian Chen) and Bioengineering Laboratory (Director: Dr. Joseph Crisco). It occupies approximately 20,000 square feet of laboratory and office space on the 4th floor of the Coro West Building of Rhode Island Hospital.

**The Cell and Molecular Biology Laboratory** is fully equipped for cell culture and routine biochemical, molecular biology, and biomechanical testing procedures, including biochemical core lab, microscope and image analysis lab, histology core lab, and molecular biology core lab. A cold room, ice machine, glass washing, fume hoods, two dark rooms, and two storage room are also located within the laboratory. In addition,

the laboratory contains a cell culture laboratory that is certified for Biological Safety Level-2 (BSL-2) use. Additionally, it is equipped and maintained to meet these specifications, as described in the NIH Guidelines for Recombinant DNA Use. The laboratory facility includes a fully equipped Histology and Imaging Core with a full-time histologist.

**Flow Cytometry Core at Rhode Island Hospital:** The core is located in newly renovated laboratory space and equipped with cutting edge instrumentation such as a BD Bioscience Influx cell sorter equipped with a 200mW 488 nm sapphire, 100mW UV, 50mW 405 nm violet, 30mW 635 nm red, and 75mW 561 nm green/yellow lasers. This sorter is capable of carrying out cell separations, single cell deposition into 96 well plates and is housed within a biosafety cabinet

### **LIFESPAN RESEARCH ADMINISTRATION**

The Office of Research Administration at Lifespan provides epidemiological consultation, database development, training and compliance, statistical analysis, outcomes measurement, IRB submission and data entry and data management support.